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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/963,693	09/25/2001	Gary Ruvkun	00786/351006	2040

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EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/963,693	RUVKUN ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *21 October 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☒ Applicant's reply has overcome the following rejection(s): Prior art rejection under 35USC 102, claim 2 is cancelled.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1 and 3*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

JEFFREY FREDMAN
PRIMARY EXAMINER
1/13/05

Continuation of 5. does NOT place the application in condition for allowance because: Claims 1 and 3 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the same reasons of record as set forth in the office action mailed on 04/19/04.
Invention relates to a method of diagnosing impaired glucose tolerance condition and obesity in a patient by analyzing the level of PTEN expression or lipid phosphatase activity.
RESPONSE TO ARGUMENTS
The applicant argues that teaching of Hirosumi, Shulman, Lonnqvist, Fontaine, Kahn and Ogg et al do not support that invention as claimed is not enabled. The applicant argues that the claimed methods are directed to diagnosis of an impaired glucose tolerance condition, obesity, or a propensity thereto and these methods do not require a complete understanding of the insulin signaling pathway, but rather require that the level of PTEN expression or activity, relative to a control, be indicative of an impaired glucose tolerance condition or obesity. The applicant argues that Ogg (1998) teaches the role of PTEN in insulin signaling, Stiles et al PNAS 101:2082, 2004 and Butler (Diabetes 51:1028, 2002) provides evidence that PTEN functions in mammalian homeostasis. The applicant argues that the instant specification teaches that a reduction or an increase in PTEN expression or function can be used in diagnosing an impaired glucose tolerance condition, obesity, or a propensity thereto in a patient, as is presently claimed. The applicant argues that Butler and Stiles (which is a post filing art) simply confirms the role of PTEN in mammalian insulin signaling, and thereby supports applicants' argument that the specification enables the present diagnosis. The applicant concluded that the specification teaches an assay for PTEN lipid phosphatase activity, therefore it would not require undue amount of experimentation to practice the invention as claimed
However, applicant's arguments are found NOT persuasive. Applicant's argument alone cannot take place of evidence lacking in the record. The scope of invention as claimed is not limited to method of diagnosing impaired glucose tolerance condition but encompasses method of diagnosing obesity in a patient by analyzing the level of PTEN expression or lipid phosphatase activity. Besides a hypothetical model, the specification as filed fails to provide a single working example, which establishes that PTEN modulates mammalian insulin signaling and/or obesity. Under the law, the disclosure "shall inform how to use, not how to find out how to use for themselves." See In re Gardner 475 F.2d 1389, 177 USPQ 396 (CCPA 1973). As stated earlier applicant's argument that Butler et al. (Diabetes 51:1028-1034, 2002) and Stiles et al PNAS101: 2082, 2004 teaches that PTEN modulates mammalian insulin signaling has been found unpersuasive because each patent application is examined on its own merit and is considered enabled in view of its own disclosure. The issue is not whether the other application support their claims but whether one supports its claims "[i]t is immaterial whether similar claims have been allowed to other" In re Gialito 188USPQ 645,648 (CCPA 1976). Considering the state of the art the specification as filed fails to provide a single working example, which establishes that PTEN modulates mammalian insulin signaling and/or is associated with the development of obesity.
The earlier office action clearly reflects the state of the art teaching that development of impaired glucose tolerance and obesity is multi-factorial and complex. For example obesity is not only the result of genetic variations but is also the out come of personal behavioral and life style (see Lonnqvist). Regarding impaired glucose tolerance the earlier office action clearly provides the evidence, which establishes the unpredictability in the art. For example GLUT4, FFA, leptin and TNF- are likely candidates that are know to affect glucose homeostasis (see Khan et al). Furthermore defects in glycogen synthase, hexokinase II, and glucose transport have also been implicated in the loss of muscle glycogen synthesis in type-2 diabetics. In addition increased plasma free fatty acid concentrations are typically associated with many insulin-resistant states, including obesity and type-2 diabetes mellitus (see Shulman et al). In addition even though activation of PI3K is necessary for full stimulation of glucose transport by insulin, emerging evidence suggests that it is not sufficient and another pathway may also be necessary. The signals downstream of PI3K are still unknown, and there is controversy as to whether the serine/threonine kinase Akt/protein kinase B (PKB) or the protein kinase C (PKC) isoform / mediates insulin stimulation of glucose transport. The pathways that mediate insulin's metabolic effects diverge downstream of PI3K and show differential sensitivity to varying levels of insulin (see Khan et al). The applicant fails to consider the complexities involved in the mammalian insulin signal transduction pathway especially in context with impaired glucose tolerance and the development obesity. For example it is unclear how one skill in the art would diagnose impaired glucose tolerance or obesity or propensity thereto by analyzing PTEN lipid phosphates activity alone in type-diabetic patients, wherein the impaired glucose tolerance is the result of loss of insulin secretion. The applicant fails to provide any evidence that analysis of PTEN expression or activity in would diagnose impaired glucose tolerance condition in type-1 diabetic patients. The examples provided in the specification are prophetic and read as instructions rather than examples, leaving significant amount of experimentation necessary to practice the invention. The USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise. It is noted that patent protection is granted in return for an enabling disclosure of an invention, no for vague intimations of general ideas that may or may not be workable (See Brenner v. Manson , 383 U.S. 519, 536, 148 USPQ 689, 696 (1966), Stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
In instant case the specification as failed to establish the role of PTEN in mammalian glucose homeostasis and/or obesity. Diagnosis of impaired glucose tolerance condition and obesity by analyzing PTEN lipid phosphatase activity in any and all tissues sample is not considered routine in the art and without sufficient guidance to role or PTEN in glucose homeostasis and/or obesity, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore considering the unpredictability in the art and the limited guidance provided in the specification as filed one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed. The undue experimentation required would include scientific evaluation of the role of PTEN in impaired glucose tolerance and obesity especially in context with the multi factorial nature of these disorders.